

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: TERESA STANEK REA  
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ALEXANDRIA, VIRGINIA 22313-1404

## PCT

### NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

**24 OCT 2003**

Applicant's or agent's file reference

035388-533

#### IMPORTANT NOTIFICATION

International application No.

PCT/US03/00373

International filing date (day/month/year)

08 JANUARY 2003

Priority Date (day/month/year)

09 JANUARY 2002

Applicant

ELAN PHARMACEUTICALS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Authorized officer

*Valerie Bell-Hamilton*  
GODLAMUDI S. KISHORE

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 27 OCT 2003

WFO

PCT

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>033388-533   | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |   |
| International application No.<br>PCT/US03/00373   | International filing date (day/month/year)<br>08 JANUARY 2003  | Priority date (day/month/year)<br>09 JANUARY 2002 |
| International Patent Classification (IPC) or national classification and IPC<br>IPC(7): A 61K 9/127 and US Cl.: 424/450; 264/4.1, 4.3 |  |   |
| Applicant<br>ELAN PHARMACEUTICALS, INC.   |  |   |

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1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

|  |  |
|--|--|
| Date of submission of the demand<br>30 JULY 2003   | Date of completion of this report<br>24 SEPTEMBER 2003                       |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231 | Authorized officer<br><i>Valerie Ball-Harris for</i><br>GOLLAMUDI S. RISHORE |
| Facsimile No. (703) 305-3230   | Telephone No. (703) 308-1235   |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/00373

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

☒ the international application as originally filed

☒ the description:

pages 1-22 , as originally filed  
 pages NONE , filed with the demand  
 pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 23-52 , as originally filed  
 pages NONE , as amended (together with any statement) under Article 19  
 pages NONE , filed with the demand  
 pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages NONE , as originally filed  
 pages NONE , filed with the demand  
 pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages NONE , as originally filed  
 pages NONE , filed with the demand  
 pages NONE , filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

### 5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US03/00373

**II. Priority**

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
  - ☐ translation of the earlier application whose priority has been claimed.
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☐ claims Nos. \_

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US09/00973

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 13.2, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☐ the parts relating to claims Nos. .

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International application No.

PCT/US03/00373

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

|                               |                     |     |
|-------------------------------|---------------------|-----|
| Novelty (N)                   | Claims <u>1-154</u> | YES |
|                               | Claims <u>NONE</u>  | NO  |
| Inventive Step (IS)           | Claims <u>NONE</u>  | YES |
|                               | Claims <u>1-154</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-154</u> | YES |
|                               | Claims <u>NONE</u>  | NO  |

**2. citations and explanations (Rule 70.7)**

Claims 1-8, 10-13, 20-26, 30-38, 40-43, 50-60 and 62-154 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al (US 5,741,513).

GHYCZY et al disclose a method of preparation of liposomes. The method involves the use of already formed liposomes and then adding an aqueous buffer and an alcohol to produce once again a liposomal population which is self-preserving, storable and transparent. The liposomes can encapsulate a variety of biological agents (note the abstract, col. 3, line 24 through col. 6, line 32, Examples and claims). GHYCZY et al differs from instant method in that according to instant method, the aqueous medium is added in aliquots or stages (step C in claim 1 for example) whereas in GHYCZY et al, all of the aqueous medium is added in one step. However, since both methods lead to the formation of liposomes, instant method wherein the aqueous medium is added in steps is an obvious manipulation of the basic method taught by GHYCZY et al to obtain the best possible results.

Claims 9,39 and 61 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above in view of IGA et al (US 4,877,561). What is lacking in GHYCZY et al is the teaching of the use of acetone instead of alcohol as the volatile organic solvent.

IGA et al while disclosing a liposome gel formulations containing a variety of drugs teach that for the formation of liposomal gels organic solvents such as alcohols and acetone can be used (abstract, col. 1, line 63 through col. 3, line 34).

The use of acetone instead of alcohol taught by GHYCZY et al would have been obvious to one of ordinary skill in the art since the reference of IGA et al shows that acetone could be used instead of an alcohol.

Claims 13-19, 27-29 and 43-49 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above in view of KIRPOTIN et al (US 5,980,935). What is lacking in GHYCZY (Continued on Supplemental Sheet.)

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/USOs/00s73

## VI. Certain documents cited

### 1. Certain published documents (Rule 70.10)

Application No.  
Patent No.

Publication Date  
(day/month/year)

Filing Date  
(day/month/year)

Priority date (valid claim)  
(day/month/year)

### 2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure  
(day/month/year)

Date of written disclosure  
referring to non-written disclosure  
(day/month/year)



**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US03/00373

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-154 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the independent claims are indefinite for the following reason(s): These claims recite 'liposomes are prepared by a method other than the instant method'; this expression is not a positive expression.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/00873

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

et al are the teachings of nucleic acids and plasmids as the active agents. The use of nucleic acids and plasmids as the active agents however, would have been obvious to one of ordinary skill in the art since the reference of KIRPOTIN et al shows that these agents are routinely incorporated in liposomes for transfection (note the abstract and Examples).

Claims 1-154 meet the criteria set out in PCT Article 33(2) and (4), because the prior art does not specifically teach a method containing instant steps and since the invention finds its utility in the delivery of a variety of active agents.

\_\_\_\_\_  
**NEW CITATIONS**  
\_\_\_\_\_

US 4,877,561 A (IGA et al) 31 OCTOBER 1989, see abstract, col.2, line 42 through col. 3, line 64.

## PATENT COOPERATION TREATY

## PCT

## NOTE ON INFORMAL COMMUNICATION WITH THE APPLICANT

(PCT Rule 66.6)

|   |   |   |
|---|---|---|
| International application No.<br>PCT/US03/00373 | Applicant's or agent's file reference<br>033388-533 | Date of informal communication<br>(day/month/year)<br>11 SEPTEMBER 2003 |
|---|---|---|

Applicant  
ELAN PHARMACEUTICALS, INC.

|   |   |   |  |   |
|---|---|---|--|---|
| <u>Communication</u><br><input checked="" type="checkbox"/> by telephone<br><input type="checkbox"/> personal | <u>Participants</u><br><input checked="" type="checkbox"/> Applicant: NONE<br><input checked="" type="checkbox"/> Agent: Teresa Rea<br><input checked="" type="checkbox"/> Examiner(s): GOLLAMUDI S KISHORE | <input type="checkbox"/> identity checked | <input type="checkbox"/> authorization checked | <input type="checkbox"/> personally known |
|---|---|---|--|---|

Summary of communication:

The authorization for skipping the written opinion (408) and sending directly 409 was discussed. The attorney agreed for a 409.

☐ An extension of time limit is granted (Form PCT/IPEA/427).

☒ A copy of this note is being sent to the applicant with Form PCT/IPEA/429.  
PCT/IPEA/424.

|                               |  |
|-------------------------------|--|
| Applicant/Agent<br>Teresa Rea | Authorized officer of IPEA/US<br><i>Valerie Bed-Herrera</i><br>GOLLAMUDI S KISHORE<br>Telephone No. (703) 308-1235 |
|-------------------------------|--|

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